REMARKS

Support for new Claim 36 can be found, *inter alia*, at page 2, lines 4-9 of the present specification.

On page 2 of the Office Action, the Examiner maintains the rejection of Claims 31-33 under 35 U.S.C. § 112, as lacking enablement.

Specifically, the Examiner states that while the specification is enabling for a hydroxylated triple helical protein wherein the protein is a collagen, such does not provide enablement for the broad scope of polypeptides encompassed by the claims.

In view of the amendments to the claims to limit such to a polypeptide or peptide selected from the group consisting of collagens, collagen fragments, and collagen-like proteins, Applicants respectfully submit that the Examiner's rejection has been rendered moot.

On page 5 of the Office Action, the Examiner maintains the rejection of Claims 31-35 under 35 U.S.C. § 112, first paragraph, as failing to meet the written description requirement.

Specifically, the Examiner states that the specification fails to provide support for the *proviso* "at least one of m and o is 1".

In view of the amendments to the claims to delete the *proviso*, Applicants respectfully submit that the Examiner's rejection has been rendered moot.

On page 8 of the Office Action, the Examiner maintains the rejection of Claims 31-35 under 35 U.S.C. § 102(e) as being anticipated by St. Pierre et al.

Specifically, the Examiner notes that Applicants have limited the claimed polypeptides to "recombinant" polypeptides, and that Applicants argue that in St. Pierre et al, the peptides are synthesized by a chemical synthesis protocol, as opposed to being recombinantly produced. However, the Examiner finds this argument unpersuasive.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

St Pierre et al is concerned with artificial collagen comprising a stabilized ordered triple helix of copolypeptide strands containing repeating amino acid triads of the formula $(X_{aa}\text{-}X_{bb}\text{-}Gly)\text{-}(X_{aa}\text{-}X_{bb}\text{-}Gly)_n\text{-}(X_{aa}\text{-}X_{bb}\text{-}Gly)\text{-}$. The collagen may be modified with groups which improve its physical and chemical properties for the intended use, such as adhesive and cross-linking groups.

At column 3, lines 29 *et seq.*, St Pierre et al indicates that the invention described therein, like native collagen, is biocompatible:

> ...but are of a simplified oligopeptide structure which can be easily synthesised in a laboratory or commercial quantities; the compounds herein also referred to as "collagen mimics", can also be genetically engineered as fusion proteins/polypeptides employing techniques well-known in the art... (emphasis added)

Applicants submit that it is clear from the quoted passage that the reference to "genetically engineered as fusion proteins/polypeptides" is to the "collagen mimics". The

"collagen mimics" are described at column 3, lines 61-67, as being characterized by a core comprising an ordered triple helix of at least three copolypeptide strands of repeating amino acid triads (X_{aa}-X_{bb}-Gly), each strand being linked at the C-terminal end thereof to a common template for stabilization of the helical secondary structure.

At column 4, lines 13-18, St Pierre et al states:

> The core may also be modified by a polymer for altering the biophysical or biochemical properties of the mimic, covalently linked to the distal end of one or more of the peptide strands or adhesive moiety (AM), or to functional groups on the strand or adhesive moiety backbones, or to the template.

Applicants submit that it is clear from the above statement in St. Pierre et al that the "polymer" is additional to the core, but does not form part of the core (i.e., the collagen mimic).

At column 5, line 41-64, St Pierre et al states:

> In so-modified collagen mimics of the invention, a polymer is included to increase the molecular weight of the mimic, and/or to vary other properties of the mimic such as hydrophilicity, immunogenicity, and *in vivo* stability. As indicated in Formula A by "•", the polymer may be activated at one end thereof and grafted to the distal end of one or more of the peptide strands; to the distal end of the adhesive moiety; to the backbones of the strands or adhesive moiety; to the spacer; or to the template by covalent linkage of the activated groups to appropriate functional side chains or terminal groups of the mimic, especially amino or hydroxy groups. The polymer may also be activated at both ends for cross-linking of the mimic, particularly cross-linking of the peptide strands. Generally, the molecular weight of the polymer is from about 200 to 100,000 daltons, preferably at least about 1,000 daltons. Polyethylene glycol, especially

> monomethoxypolyethylene glycol, is a particularly suitable polymer for clinical use because of its known efficacies and safety as a protein modifier (*supra*). Polyvinyl alcohol, polyglutamic acid, polyaspartic acid, polylysine, or Pluronics™ polymers are also exemplary. The polymer may also be selected for its biodegradability, biocompatibility, benign reactivity with the mimic, and other properties as desired.

It is clear from this passage that St Pierre et al teaches that the "polymer", if used to modify the collagen mimics of the invention, is to be activated and grafted onto, *inter alia*, the peptide strands. However, there is no teaching or suggestion in this passage of recombinantly producing both the collagen mimic and the polymer.

The Examiner asserts that St Pierre et al "... teaches that this polymer can be a peptide selected from polyglutamic acid, polyaspartic acid and polylysine, which meets the claim limitation of at least one peptide domain which is heterologous to collagen proteins which do not comprise a triple helical forming repeating sequence".

However, the passage cited above indicates that polyethylene glycol, especially monomethoxypolyethylene glycol, is a particularly suitable polymer for clinical use. Indeed, the use of polyethylene glycol is described in detail at column 3, lines 3-17 in St. Pierre et al to the related art. It also cites as suitable polymers, polyvinyl alcohol and "Pluronics™ polymers" (polymers based on ethyleneoxide and propylene oxide - see attached BASF product information).

Furthermore, all three Examples provided in St Pierre et al involve the use of a polymer or copolymer of polyethylene glycol

as the polymer. All three Examples are prepared by chemical reaction, including the triads.

Polyethylene glycol, polyvinyl alcohol and "Pluronics™ polymers" cannot be produced recombinantly.

The Examiner also refers to the passage at column 6, lines 24-34 which indicates that the oligopolypeptide strands that are comprised of the triple helical forming repeating sequence can be prepared as fusion proteins or peptide fragments thereof from appropriate genetically-engineered expression vectors in suitable host cells. However, that passage, is concerned with "the oligopeptide", which would not be considered by the skilled artisan to include the "polymer" which has been added by modification. Rather it would be understood by the skilled person to be a reference to the core oligopeptide structure (see column 3, lines 37-40), that is, the collagen mimics.

Thus, St Pierre et al, at most, suggests the possibility of recombinantly producing the "collagen mimics" characterized by a core comprising an ordered triple helix of at least three copolypeptide strands of repeating amino acid triads (X_{aa}-X_{bb}-Gly). There is absolutely no teaching or suggestion of producing anything other than the core by recombinant techniques.

In any event, insofar as St. Pierre et al suggest recombinant production of the core, it provides no details on how to produce the core recombinantly. In particular, St. Pierre et al is completely silent on the need to ensure that any recombinant technique is such that there is hydroxylation

and Applicants respectfully disagree with the Examiners contention that this would be inherent.

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested by St. Pierre et al, and thus request withdrawal of the Examiner's rejection.

In view of the amendments to the claims, and the arguments set forth above, reexamination, reconsideration and allowance are respectfully requested.

The Examiner is invited to contact the undersigned at his Washington telephone number on any questions which might arise.

Respectfully submitted,

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